



# AMENDMENTS TO THE SPECIFICATION:

Please amend the paragraph spanning page 9, line 19 and page 10, line 4 as shown below:

**Fig. 3. Comparison of dUSP and hRXR ligand binding domains.** (A) Selected contacts made between 9-cis RA and residues in the hRXR $\alpha$  ligand-binding pocket as determined from cocrystals (4.2 Å or less, from Egea et al. (2000) EMBO J. 19, 2592-2601). On the left is also shown a conformation of epoxyfarnesoic acid, exhibiting similarities between its structure and that of the terpenoid backbone and carboxyl group of 9-cis retinoic acid. (B and C) RASMOL-generated ribbon diagrams for the ligand-binding domains of the hRXR $\alpha$  and dUSP, respectively. (B) This shows in the hRXR $\alpha$  ligand-binding pocket the structure of the ligand 9-cis retinoic acid (carbon backbone in light blue, terminal carboxylate oxygens in dark blue, adapted from Egea et al. (2000) EMBO J. 19, 2592-2601). (C) This shows methyl epoxyfarnesoic acid (yellow carbon backbone and blue terminal carboxylate oxygens) lain manually in the dUSP ligand-binding pocket with the carboxy and distal (epoxy) ends, respectively, situated in similar regions of the pocket as the carboxyl end and distal end of 9-cis RA in hRXR $\alpha$ . (D) An overlay of the dUSP and hRXR ribbon diagrams of B and C, with emphasis (white arrows) on the similar placement of Gln275, Trp305, Leu326, Cys432 and His435 in hRXR as compared to Gln288, Trp318, Leu367, Cys472 and His475 in dUSP.

Please amend the paragraph spanning page 11, line 24 and page 12, line 5 as shown below:

**Fig. 6. Fluorescence response of wild-type and P498W/P499W mutant USP to farnesoid ligands.** (A) The location of the mutational placement of the two tryptophan residues at the end of (red-colored)  $\alpha$ -helix 12. USP also possesses two natural tryptophan residues on helix 5 (W318, shown in green extending into pocket; W328, not shown, extending out of pocket). (B) Methyl epoxyfarnesoate binding to wild-type USP results in suppression of receptor fluorescence, while farnesol and ethanol carrier do not have that effect. (C) Methyl epoxyfarnesoate binding to P498W/P499W mutant results in a very different pattern of fluorescence response than wild-type USP in B, evidencing that  $\alpha$ -helix 12 moves in its relative location upon USP binding of methyl epoxyfarnesoate. The wild-type USP and P498W/P499W similarly bound in part as monomer and in part as dimer to a DR12 probe in gel shift assay,

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evidencing that the P498W/P499W mutations did not affect receptor structure globally (not shown).

**Please delete Figures 7-9 and the references thereto on page 12, lines 6-7.**